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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,574	02/01/2007	Jeffrey T. Borenstein	61947(51588)	6443
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EXAMINER				
FORD, ALLISON M				
ART UNIT		PAPER NUMBER		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/568,574

Applicant(s)

BORENSTEIN ET AL.

Examiner

ALLISON M. FORD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 June 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 9-12, 25 and 26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 13-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-942)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicants' response of 6/9/2010 has been received and entered into the application file. Claim 8 has been amended, new claims 25 and 26 have been added. All arguments have been fully considered, and are each addressed below, as appropriate.

Election/Restrictions

The instant application is a national stage entry under 35 USC 371, and thus was subject to the unity of invention requirement as set forth in 37 CFR 1.475. Pursuant to 37 CFR 1.475(e) a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories ('groups'):

- (1) A product and a process specially adapted for the manufacture of said product; or
- (2) A product and process of use of said product; or
- (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
- (4) A process and an apparatus or means specifically designed for carrying out the said process; or
- (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

The initial application was found to contain two inventive groups: a product and to a process specially adapted for the manufacture of said product; unity of invention was not found be lacking a posteriori because the two inventions did not share a special technical feature which provided a contribution over the prior art.

New claims 25 and 26 are directed to different products/apparatuses from that originally elected, and therefore lack unity of invention a priori.

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Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 25 and 26 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b).

Claim Objections

The amendment to claim 8 obviates the objection previously made thereto.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Applicants have traversed the rejection of record under 35 USC 102(b) over Clark et al on the grounds that the micromachined substrates of Clark et al only provide for organization of a single cell type into subassemblies (i.e. the grooves), whereas the instant claims require multiple cell types to be organized into subassemblies.

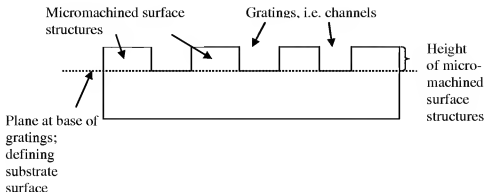
In response, Applicants' arguments have been fully considered, but are not found persuasive. It is respectfully submitted that Applicants are arguing limitations not in the presently examined claims. Specifically, none of claims 1-5, 7 or 8 (those rejected over Clark et al) actually require the presence of any cell type, much less multiple cell types; rather claims 1-5, 7 and 8 (in fact all of claims 1-8) are

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directed to a substrate per se, not a substrate with multiple cell types present thereupon. The ability of a substrate to support and organize multiple cell types into subassemblies is considered an intended use of the claimed substrate. Intended use limitations are considered only insofar as the intended use limits or defines the structure of the product. In the instant case, though Clark et al only exemplify providing a single cell type on each of the micromachined substrates, Clark et al does show that the substrate is capable of supporting growth of different cell types (i.e. Clark et al shows the substrate can separately support growth of BHK cells, MDCK cells and chick embryo cells), and further that the micromachined grooves controls the position of the cells on the substrate.; therefore it is reasonable to conclude that the micromachined substrate of Clark et al could support multiple cell types on a single substrate- where the different cell types are seeded onto separate grooves. Thus the substrate of Clark et al is maintained as anticipating the substrate of instant claims 1-5, 7 and 8.

Claims 1-5, 7 and 8 stand rejected under 35 USC 102(b) as being anticipated by Clark et al (J Cell Sci, 1991).

Clark et al disclose quartz slides (a substrate) having gratings produced therein, the gratings had depths ranging from 100 nm to 400 nm (See Clark et al, pg. 75, Fig. 2). The gratings were produced by photolithography methods (See Clark et al, Pg. 73-75 "Materials and Methods: Pattern definition"). The plane at the bottom of the gratings is considered to read on the substrate, the positive space between the gratings is considered to read on micromachined surface structures which define the walls and floor of a microchannel. Because the gratings have a depth of 100-400 nm, the micromachined surface structures can be considered to comprise nanotopographical features:



Clark et al teach that BHK, MDCK and chick embryo cells grew on the slides, orienting along the gratings (i.e. laterally) (See Clark et al, Pg. 74 "Results: Cell alignment"), therefore the micromachined substrates are capable of supporting growth of multiple types of cells (i.e. able to 'preferentially adhere' one or more cell types to a desired location on the substrate). As discussed above, the instant claims do not require multiple cell types to be present on the same substrate, but rather only require that the substrate be capable of organizing multiple cell types into desired subassemblies within the micromachined surface structures; because the micromachined surface structures in the quartz slides of Clark et al are capable of orienting a variety of cell types into different subassemblies, it is reasonable to conclude that the micromachined surface structures would be capable of orienting multiple cell types into different subassemblies, one cell type being seeded in each grating. Therefore the substrate of Clark et al anticipates claims 1-5, 7 and 8.

Applicants have traversed the rejection of record under 35 USC 102(b) as being anticipated by Desai et al on the grounds that Desai et al fails to disclose use of nanotopographical features to organize multiple cell types into subassemblies.

As discussed above with respect to Clark et al, claim 1 and dependents thereof do not require multiple cell types to actually be present, rather the claims are only to the substrate per se, and thus the

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arguments are not persuasive with regards to claim 1. Claim 13 does require multiple cell types to be present, and thus the argument is persuasive with regards to claim 13. However, upon reconsideration the rejection based on Desai et al is **withdrawn** in its entirety, for insufficiency of teachings.

The following is a new grounds of rejection being set forth:

Claims 1-8 and 13-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Vacanti et al (US 2007/0281353).

The applied reference has at least a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Vacanti et al disclose a three-dimensional system comprising at least two layers, wherein each layer comprises channels divided longitudinally into two compartments by a centrally positioned membrane, each compartment can comprise a different cell type. Each layer further comprises a support element, comprising a surface in which the channels are formed, and which defines the walls and floor of the channels (See Vacanti et al, ¶0050-0052). The system can be produced via a lithography process (See Vacanti et al, ¶0053-0055). The membrane which divides the channels into two compartments is preferably porous, the pores are nanosized (See Vacanti et al, ¶0085).

The support element is considered to read on a substrate having micromachined surface structures provided thereon. The nanoporous membrane, provided on the support element, is considered to read on nanotopographic features superimposed on the support element. The orientation of the membrane is such that it organizes multiple cell types into desired subassemblies (i.e. separates vascular cells from parenchymal cells).

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Different cell types, including combinations of hepatocytes and fibroblasts, are specifically taught to be provided within the compartments of a single channel (See Vacanti et al, claim 35). A pumping means can further be included in the device to circulate fluid through the device (See Vacanti et al, claim 36). The system can further comprise lines in fluid communication for excretion removal (See Vacanti et al, ¶0106). Therefore the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Applicants have traversed the rejections of record under 35 USC 103(a) as being unpatentable over Desai et al, in view of Borenstein, and US Patent 5,665,596, for the reasons discussed above with respect to Desai et al, and further that the subsequent references fail to remedy the deficiency.

The rejection is **withdrawn**.

Upon reconsideration the following new grounds of rejection is set forth:

Claims 1-8 are rejected under 35 USC 103(a) as being unpatentable over Clark et al (J Cell Sci, 1991).

The teachings of Clark et al are set forth above and have been shown to anticipate claims 1-5, 7 and 8. Clark et al differs from the substrate of claim 6 only with regards to the orientation of the gratings, Clark et al teaches the gratings (which read on nanotopographical features) as being parallel lines, whereas claim 6 requires the nanotopographical features to be oriented in a grid.

It is submitted that because Clark et al was focused on observing the effect of topographical features on cell growth and orientation, and they did observe that a variety of different cells would orient in a generally straight line along the pattern of a straight grating, it would have been prima facie obvious to one having ordinary skill in the art to then test if the cells were able to follow the pattern of curved or torturous pathways, to test the limits of cells interactions with the substrate topography. The formation of a grid pattern (i.e. intersecting grating lines) would provide such a torturous pathway. Methods for forming the gratings (nanotopographical features) are clearly taught by Clark et al, thus it is submitted that modification of the micromachined substrate of Clark et al to comprise intersecting grating lines would have been within the purview of the skilled artisan as well. Thus, because one would have had reason to produce a substrate having a grid-like pattern of nano-sized grating lines, and means for producing such a substrate having nano-sized grating lines were known to the artisan, the substrate of instant claim 6 is held as unpatentable over the substrate of Clark et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In*

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re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

It is acknowledged that Applicants' filed terminal disclaimers over applications 10/557,081, 10/187,247, and 12/058,128 (on 6/9/2010), however the terminal disclaimers were **not approved** due to failure to identify the extent ownership the assignee holds in each application.

It is noted that application 10/187,247 has been issued as US Patent 7,759,113; however, the patented claims do not define a substrate which has nanoscale features, as currently required. Therefore the obviousness-type double patenting rejection is **withdrawn** over application 10/187,247 (US Patent 7,759,113).

It is further noted that application 12/058,128 has been abandoned, thus the provisional obviousness-type double patenting rejection over that application is **withdrawn**.

Claims 1-8 and 13-24 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 6, 24, and 32-36 of copending Application No.

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10/557,081, hereafter referred to as the '081 application. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are overlapping in scope.

The instant claims recite a tissue engineering system comprising a substrate with nanoscale structures for the organization of cell types with a semi-permeable membrane, and a fluid communication system for nutrient and metabolite transport. The semi-permeable membrane may be between layers or centrally dividing a compartment. (limitations in instant claims 13-14, 16-18 and 24).

The '081 application teaches a three-dimensional system comprising at least two layers with a centrally positioned membrane separating each compartment wherein each compartment comprises different cell types and a fluid communication system ('081, claims 1 to 2, 6, 24, 32 to 36).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The following is a new ground of rejection:

Claims 1-8 and 13-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each of claims 1 and 13 the phrase "wherein said micromachined surface structures comprise nanotopographic features superimposed thereon" (emphasis added) renders the claim indefinite. It is unclear if the nanotopographic features are superimposed on the micromachined surface structures, or if the nanotopographic features are the micromachined surface structures and are superimposed on the substrate. In other words, are the micromachined surface structures one and the same as the

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nanotopographic features, or are the micromachined surface structures distinct from the nanotopographic features?

In claims 4 and 20 the phrase "preferentially adhere" renders the claims indefinite, as it is a relative term with no basis for comparison. Preferentially adhere compared to what? It appears it would be remedial to replace the phrase "preferentially adhere" with "facilitate adhesion to."

Correction is required.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALLISON M. FORD whose telephone number is (571)272-2936. The examiner can normally be reached on 8:00-6 M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Allison M. Ford/
Primary Examiner, Art Unit 1651